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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/151,612	09/11/1998	LEONARD D. KOHN	5616/3	8049

7590 09/09/2002

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EXAMINER	
NGUYEN, QUANG	
ART UNIT	PAPER NUMBER
1636	23

DATE MAILED: 09/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/151,612	KOHN ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-18,21-26,29-60,62 and 67-91* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,2,4-18,21-26,29-60,62 and 67-91* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Prosecution Application

The request filed on June 19, 2002 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/151612 is acceptable and a CPA has been established.

Applicants' amendment filed on 7/1/02 in Paper No. 21 has been entered. Note that in the amendment filed on 7/1/02, there are two newly added claims both of which are numbered 85. Per 35 CFR 1.126, newly added claims "84-90" have been renumbered as claims 84-91.

Claims 1-2, 4-18, 21-26, 29-60, 62, 67-78 and 80-91 are pending in the present application. However, upon reviewing the application and after taken into account of Applicants' amendment filed on 7/1/02, it would have required undue burden for the Examiner to search and consider the patentability for all the pending claims. For Applicants' convenience, following is the election/restriction requirement including claims drawn to inventions that are not elected by Applicants without traverse in Paper No. 8 dated 1/20/00. It is noted that claim 33 is dependent on the cancelled claim 28; therefore the nature of this claim is not clearly determined to be restricted in the following groups.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

Group Restriction:

I. Claims 1-2, 4-18, 21-26, 29-32, 34-35, 42-46, 60, 62, 74-76, and 81-91, drawn to methods of increasing immune recognition of a mammalian cell (non-immune and/or immune cells) in a subject; methods for presenting antigen to the immune system of a mammal in need of immunotherapy or for treating a mammalian disease which is sensitive to immunotherapy utilizing cells obtained from the subject or the mammal, that have been transfected with a sequence non-specific double-stranded polynucleotide greater than 25 nucleotides; and a vaccine for treating cancer comprising a somatic mammalian cell with the enhanced ability to present antigen to the immune system containing a sequence non-specific double-stranded polynucleotide greater than 25 nucleotides in length, classified in class 424, subclass 93.21.

II. Claims 77-78, 80 and 89-91, drawn to a vaccine for treating cancer comprising an adjuvant comprising a sequence non-specific double-stranded polynucleotide greater than 25 nucleotides in length, an antigen of interest, a pharmaceutically acceptable carrier; and a method for augmenting a vaccine response using the same, classified in class 514, subclass 44.

III. Claims 36-39 and 55-56, drawn to a screening method for a drug that regulates antigen presentation or a method of screening a compound that regulates the effect of double-stranded polynucleotides utilizing a mammalian cell containing an exogenous double-stranded polynucleotide

in the presence or absence of the drug or the compound, classified in class 435, subclass 7.2.

IV. Claim 40, drawn to a pharmaceutical composition comprising an effective amounts of Methimazole, methimazole derivatives or tautomeric cyclic thiones, classified in class 424, subclass 900.

V. Claim 41, drawn to a DNA molecule comprising at least one of SEQ ID NOs: 1-16, classified in class 536, subclass 23.1.

VI. Claims 47-54, drawn to a method of identifying differential expression of a a sequence expressed in response to a double-stranded polynucleotide comprising isolating and comparing RNA sequences of treated and non-treated cells, classified in class 435, subclass 6.

VII. Claims 57-59, drawn to methods of screening for a compound that regulates the effect of double-stranded polynucleotides utilizing an animal immunized with a non-professional immune cell transfected with an antigen and a double-stranded polynucleotide in the presence or absence of a compound, classified in class 424, subclass 9.2; class 435, subclass 6.

VIII. Claims 67-73, drawn to a method to assess viral replication comprising measuring and comparing the level of expression of a gene which is affected by transfection with double-stranded polynucleotides in a cell with that in cells which are known to not have been infected by the virus, classified in class 435, subclass 6.

The inventions are distinct each from the other for the following reasons:

Although there are no provisions under the section for "Relationship of Inventions" in M.P.E.P. § 806.05 for inventive groups that are directed to different methods, restriction is deemed to be proper because the methods in Groups I, II, III, VI, VIII and VIII appear to constitute patentably distinct inventions for the following reasons: These methods are directed to methods that are distinct both physically and functionally, and are not required one for the other. Invention I requires the introduction of a mammalian cell (immune and nonimmune cell) containing a sequence non-specific double-stranded polynuleotide greater than 25 nucleotides in length into a subject for increasing immune recognition of the mammalian cell or for treating a mammalian disease (an *ex vivo* gene therapy); Invention II requires the introduction of a sequence non-specific double-stranded polynucleotide greater than 25 nucleotides in length together with an antigen into a host for augmenting a vaccine response; Inventions III is drawn to a screening method for a drug or a compound that regulates antigen presentation utilizing a mammalian cell containing an exogenous double-stranded polynucleotide in the presence or absence of the drug or compound; Invention VI is directed to a method of identifying differential expression of a sequence expressed in response to a double-stranded polynuleotide comprising isolating and comparing RNA sequences of treated and non-treated cells; Invention VII is drawn to method of screening for a compound that regulates the effect of double-stranded polynucleotides utilizing an animal immunized with a non-professional immune cell transfected with an antigen and a double stranded polynucleotide in the presence or absence of a

compound; and Invention VIII is drawn to a method to assess viral replication in a cell comprising measuring and comparing the level of expression of a gene which is affected by transfection with double-stranded polynucleotides in a cell with that of a cell which is known not being infected by the virus. These methods involve different steps, different starting materials and different technical considerations in achieving different intended desired end-results (therapeutic and non-therapeutic results). Additionally, the vaccine composition of Group I, the vaccine composition of Group II, the pharmaceutical composition of Group IV and the DNA molecule of Group V are substantially different in structure and properties. For examples, none of the compositions of Groups I, II need to possess the recited SEQ ID NOs., and the methimazole, methimazole derivatives or tautomeric cyclic thiones of Group IV possess distinct chemical structures and properties from a mammalian cell containing a sequence nonspecific double-stranded polynucleotide greater than 25 nucleotides in length of Group I, or a composition comprising an antigen and a sequence non-specific double-stranded polynucleotide greater than 25 nucleotides in length of Group II.

It is noted that claims 89-91 are dependent claims reciting the above patentably distinct methods of treating cancer using distinct vaccine compositions, and distinct methods for augmenting a vaccine response and for increasing immune recognition of a mammalian cell in a subject of Groups I and II, which lack unity of invention for the reasons already set forth above.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject

matter, separate search requirements, it would be unduly burdensome for the examiner to search and/or consider the patentability of all the inventions in a single application. Therefore, restriction for examination purposes as indicated is proper.

Species Restriction:

Should Applicants elect Group I, claims 1, 6, 9, 11, 13, 17-18, 21-25, 29-32, 34-35, 74-75, 42-45, 60, 62, 84 are generic to a plurality of disclosed patentably distinct species of a mammalian cell comprising:

(a) a somatic cell; (b) an antigen presenting cell; and (c) a thyroid cell.

Applicant is required under 35 U.S.C. 121 to elect a specifically named species as indicated above.

I. Should Applicants species (a) above, claims 1, 2, 6, 9, 11, 13, 16-18, 21-25, 29-32, 34-35, 42-46, 60, 62, 74-76, 81-82, 84, 89-91 are generic to a plurality of disclosed patentably distinct species comprising:

(i) a tumor cell; and (ii) a fibroblast.

Applicant is required under 35 U.S.C. 121 to elect a specifically named species as indicated above.

II. Should Applicants species (b) above, claims 1, 4, 5-9, 11, 13, 15-18, 21-26, 29-32, 34-35, 42-45, 60, 62, 74-75, 84-86 are generic to a plurality of disclosed patentably distinct species comprising:

(i) a monocyte cell; and (b) a dendritic cell.

Applicant is required under 35 U.S.C. 121 to elect a specifically named species as indicated above.

Additionally, should Applicants elect Group I, claims 1-2, 4-10, 12-18, 21-26, 29-32, 34-35, 42-46, 60, 62, 74-75, and 81-91 are generic to a plurality of disclosed patentably distinct species of introducing a sequence nonspecific double-stranded polynucleotide greater than 25 nucleotides in length into a mammalian cell comprising:

(a) transfection; (b) microinjection; (c) viral infection of the cell; (d) phagocytosis of a bacterium; (e) phagocytosis of a virus; (f) phagocytosis of a cell; (g) oncogene transformation.

Applicant is required under 35 U.S.C. 121 to elect a specifically named species as indicated above.

Additionally, should Applicants elect Group I, claims 1-2, 5-6, 9-18, 21-26, 29-32, 34-35, 42-46, 60, 62, 74-76, 81-84 and 87-91 are generic to a plurality of disclosed patentably distinct species of a sequence nonspecific double-stranded polynucleotide greater than 25 nucleotides in length comprising:

(a) the polynucleotide does not contain a stimulatory CpG motif; and (b) the polynucleotide contains one or more CpG motifs.

Applicant is required under 35 U.S.C. 121 to elect a specifically named species as indicated above.

Additionally, should Applicants elect Group I, claims 1-2, 4-15, 17-18, 21-26, 29-32, 34-35, 42-46, 74-75, 81-82, and 84-91 are generic to a plurality of disclosed

patentably distinct species of a gene or gene product associated with increased immune activation comprising:

(a) MHC class I; (b) MHC class II; (c) TAP-1; (d) TAP-2; (e) a proteosome subunit; (f) HLA-DM; (g) invariant chain; (h) RFXA; (i) B7 co-stimulatory molecule; (j) PKR; (k) MAP kinase; (l) NF-kB; (m) JAK; and (n) STAT.

Applicant is required under 35 U.S.C. 121 to elect a specifically named species as indicated above.

Additionally, should Applicants elect Group I, claim 83 is generic to a plurality of disclosed patentably distinct species of an antigen comprising:

(a) a protein; (b) a peptide; (c) an mRNA encoding antigen; and (d) a DNA encoding an antigen.

Applicant is required under 35 U.S.C. 121 to elect a specifically named species as indicated above.

Should Applicants elect Group VI, claim 41 is generic to a plurality of disclosed patentably distinct species comprising:

SEQ ID NO: 1 to SEQ ID NO:16.

Applicant is required under 35 U.S.C. 121 to elect a specifically named species as indicated above.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims

readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17 (h).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (703) 308-8339.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, Dave Nguyen, may be reached at (703) 305-2024, or SPE, Irem Yucel, at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst, Tracey Johnson, whose telephone number is (703) 305-2982.

Quang Nguyen, Ph.D.

DAVE T. NGUYEN
PRIMARY EXAMINER